Claims

1. The method of synthesizing phenstatin comprising the steps of:

oxidizing 3-(tert-butyl dimethylsilyl)oxy-4-methoxybenzaldehyde with potassium permanganate to form the corresponding carboxylic acid;

converting said carboxylic acid to the corresponding acid chloride;

treating said acid chloride with the lithium derivative obtained from 3, 4, 5-trimethoxybenzene and t-butyllithium to form a protected product;

and deprotecting said protected product to form phenstatin.

2. The method of synthesizing phenstatin prodrug comprising the steps of:

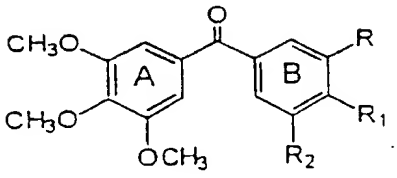
phosphorylating phenstatin with dibenzylphosphite in the presence of bromodichloromethane to form a phosphate ester;

cleaving the benzl groups from said phosphate ester by means of catalytic hydrogenolysis; and

reacting the cleaved phosphate ester with sodium methoxide to produce the phenstatin sodium phosphate prodrug.

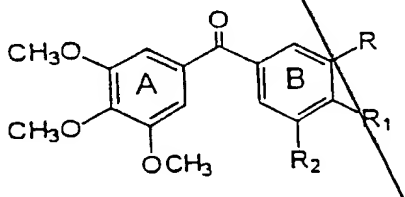
3. The method of inhibiting cancer cell growth and tubulin polymerization in an environment inflicted therewith comprising: introducing into said environment a pharmaceutically acceptable carrier and a small but effective amount of phenstatin prodrug.

4. Phenstatin prodrugs and derivatives thereof having the structure:

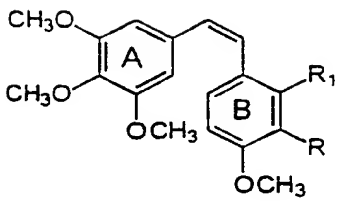


wherein when R=H and R_1 = OCH_3, R_2 is OPO_3NA_2, $OCOCH_3$, H, or OCH_3 and when R=R_2, R_2 is OCH_3, CH_3, CL or F and R_1 is H and when R_1=R_2, R_2 is OCH_3 or OCH_2O and R is H.

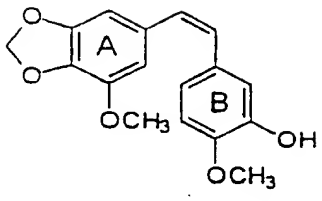
5. The method of inhibiting human cancer cell growth in a host inflicted therewith comprising administering to said host in pharmaceutically acceptable carrier a small but effective amount of a compound selected from the group consisting of phenstatin, phenstatin prodrug and the derivatives thereof having the structure.



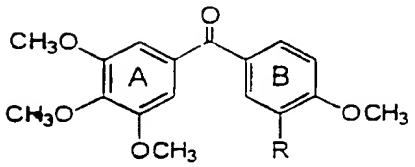
wherein when R=H and R_1 = OCH_3, R_2 is OPO_3NA_2, $OCOCH_3$, H, or OCH_3 and when R=R_2, R_2 is OCH_3, CH_3, CL or F and R_1 is H and when R_1=R_2, R_2 is OCH_3 or OCH_2O and R is H.



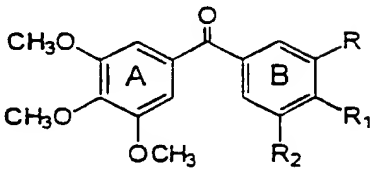
1a, R = OH, R_1 = OH
Combretastatin A-1
1b, R = OH, R_1 = H
Combretastatin A-4
1c, R = $OSi(CH_3)_2C(CH_3)_3$, R_1 = H
1d, R = OPO_3Na_2, R_1 = H
Combretastatin A-4 prodrug
1e, R = R_1 = H



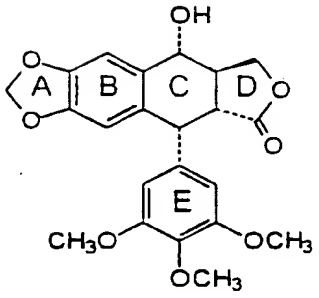
2, Combretastatin A-2



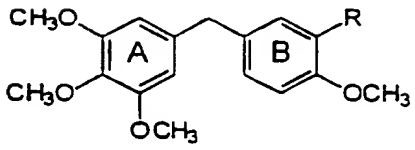
3a, R = $OSi(CH_3)_2C(CH_3)_3$
3b, R = OH, Phenstatin
3c, R = $OPO_3(C_6H_5CH_2)_2$
3d, R = OPO_3Na_2
Phenstatin prodrug
3e, R = $OCOCH_3$
3f, R = H



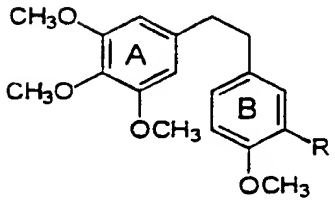
4a, R = H, R_1,R_2 = OCH_2O
4b, R = R_2 = CH_3, R_1 = H
4c, R = H, R_1 = R_2 = OCH_3
4d, R = R_2 = OCH_3, R_1 = H
4e, R = R_2 = Cl, R_1 = H
4f, R = R_2 = F, R_1 = H



5



7a, R = OH
7b, R = H



8a, R = OH
8b, R = H

Figure 1.